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RESPONSE

I. Status of the Claims

Claims 1, 3 and 4 have been amended. Claims 1-6 are therefore presently pending in the case.

II. Support for the Amended Specification and Claims

Claim 1 has been revised to further clarify the claim as suggested by the Examiner. Support for this claim can be found throughout the specification as originally filed, with particular support being found at least in claim 1 as originally filed.

Claim 3 has been revised to further clarify the claim as suggested by the Examiner. Support for this claim can be found throughout the specification as originally filed, with particular support being found at least in Claim 3.

Claim 4 has been revised to further clarify the claim as suggested by the Examiner. Support for this claim can be found throughout the specification as originally filed, with particular support being found at least in Claim 4.

As the revisions to claims 1, 3 and 4 were requested by the Examiner and are fully supported by the specification and claims as originally filed, they do not constitute new matter. Entry, therefore, is respectfully requested.

III. Formal Matters and Objections

A) Information Disclosure Statement

The International Search Report is included as reference CP on the Supplemental Information Disclosure Statement filed on August 12, 2003. All of the relevant art cited in the International Search Report also appears on the Form PTO-1449, individually. Applicants included the International Search Report on the Form PTO-1449 in the interests of full disclosure, as it demonstrates the time at which Applicants became aware of such information.

B) Title

The Final Action maintains the Examiner's objection to the title of the disclosure. While Applicants in no way agree with this objection, in order to progress the application more rapidly towards allowance, Applicants have revised the title of the present application to read: POLYNUCLEOTIDES ENCODING HUMAN GABA RECEPTORS.

C) Claims 3 and 4

The Final Action next maintains the Examiner's objection to claims 3 and 4. While Applicants do not necessarily agree with this objection, in order to progress the application more rapidly towards allowance, Applicants have revised claims 3 and 4 to read as the Examiner has suggested.

D) Claim 1

The Final Action also objects to the use of the term "at" in claim 1, and thus dependent claims 5 and 6, and suggests removal to improve the claim. In order to progress the application more rapidly towards allowance, Applicants have revised claim 1 to read as the Examiner has suggested.

E) Claims 5 and 6

The Final Action next objects to claim 5 and dependent claim 6 for the use of the use of the phrase "a nucleic acid molecule" in claim 5 and suggests that this phrase should be replaced but the phrase "the nucleic acid molecule". Applicants note that the use of the phrase "a nucleic acid molecule" in claim 5 to describe a nucleic acid molecule of claim 1 is accurate. Claim 1 reads on "An isolated nucleic acid molecule comprising a nucleotide sequence encoding an amino acid sequence ..." and due to the well-known degeneracy of the genetic code more than one nucleotide sequence can encode a single amino acid sequence. Thus, as it describes potentially more one nucleic acid sequence, the use of the phrase "a nucleic acid molecule" in claim 5 is not incorrect.

IV. <u>Rejection of Claims Under 35 U.S.C. § 101</u>

The Final Action rejects claims 1-6 under 35 U.S.C. § 101, as allegedly lacking a patentable utility due to not being supported by either a specific and substantial utility or a well-established utility.

Applicants have provided evidence that the described novel nucleic and amino acid sequences encode a protein, a human GABA receptor subunit. The function of GABA receptors are well-recognized by those of skill in the art. The Examiner disregards the evidence provided and maintains the position that the sequences of the present invention do not encode a protein with specific, substantial or a well-established utility. Additional evidence of the well-established utility of GABA receptors is provided in the form of three scientific review articles. These three reviews demonstrate the well known role of GABA receptors in human disease. The first is a recent review entitled "GABA, gamma-hydroxybuteric acid, and neurological disease" by Wong, Bottiglieri and Snead (Ann Neurol, 2003; 54 Suppl 6:S3-12). The second is a recent review entitled "GABAergic dysfunction in mood disorders" by Bambilla, *et al.*, (Mol Psychiatry, 2003 8(8):721-737) and the third is a review from 10 years ago entitled "Inherited disorders of GABA metabolism" by Jakobs, Jaeken and Gibson (J Inherit Metab Dis, 1993: 16(4):704-15). The Abstracts of these review are enclosed as **Exhibit A**.

The Final Action recognizes that Applicants have asserted that the sequences of the present invention encode a human GABA receptor, but argues that as there is no data provided to support this assertion it cannot be concluded that the sequences of the present invention encode GABA receptors and therefore any arguments regarding the function of GABA receptors are not applicable to the present case. The Final Action states (on page 3, lines 7-9 of the third paragraph) that " though Applicants suggest that the sequence(s) of the present invention encode GABA receptors, this is speculative. There is no data to support this assertion." This emphasis is misplaced as it has long been established that "there is no statutory requirement for the disclosure of a specific example". *In re Gay*, 135 USPQ 311 (C.C.P.A. 1962). Applicants' assertion of the stated utility is legally sufficient and should control the utility analysis unless the Examiner meets the burden of establishing the lack of utility by making evidence of record that conclusively refutes the Applicants' asserted utility. In the Advisory Action the Examiner submits evidence that she feels does not support Applicants' assertions, however these submissions do not refute Applicants' asserted utility. According to the Examination Guidelines for the Utility Requirement, if the applicant has asserted that the claimed invention is useful for any particular purpose (i.e., it has a "specific and substantial utility") and the assertion would be considered credible by a person of ordinary skill in the art, the Examiner should not impose a rejection based on lack of utility (66 Federal Register 1098, January 5, 2001). Thus, given the evidence previously presented by

Applicants, the skilled artisan would readily appreciate the utilities asserted by Applicants' regarding the role of the proteins encoded by sequences of the present invention, including those associated with diseases that have been linked to the novel human GABA receptor. Therefore, the present utility rejection must fail.

Despite Applicants' previous comments rebutting a small group of publications cited by the Examiner in support of the untenable position that there is no structure function relationship, the Final Action maintains that comparisons based on homology are at best speculative (page 4 lines 3-7). These articles are merely examples of a small number of spurious publications that call into doubt the usefulness of bioinformatic predictions and that Examiners have repeatedly attempted to use as a basis to deny the utility of nucleic acid sequences. However, Applicants point out that the lack of 100% unanimous agreement on the usefulness of bioinformatic prediction programs or the derivation of function using established domains and motifs is completely irrelevant to the question of whether the claimed nucleic acid sequence has a substantial and specific utility. There is, after all, a Flat Earth Society that believes that the Earth is flat not round and yet clearly the vast majority consider the Earth round. It is Applicants belief that a vast majority of those of skill in the art, as evidenced by hundreds of scientific articles, accept that there is a structure-function relationship, that is revealed by high levels of homology. Applicants respectfully point out that the legal test for utility simply involves an assessment of whether those skilled in the art would find any of the utilities described for the invention to be **believable**. Applicants submit that the overwhelming majority of those of skill in the relevant art **believe** bioinformatic prediction to be a powerful and useful tool, and that the derivation of function using established protein domains and shared motifs is often essential to defining function. The Examiner's position here and as described lines 24-26 of page 5, that homology alone is not sufficient, runs counter to that taken by the U.S.P.T.O. as described in Example 10 of the Revised Interim Utility Guidelines Training Materials (pages 53-55), which establishes that a rejection under 35 U.S.C. § 101 as allegedly lacking a patentable utility and under 35 U.S.C. § 112, first paragraph as allegedly unusable by the skilled artisan due to the alleged lack of patentable utility, is not proper when a full length sequence, and has a similarity score greater than 95% to a protein having a known function. Thus, the present utility rejection must fail as a matter of policy and a matter of law. Clearly, the position of the U.S.P.T.O. is that 95% homology to a protein having known function is sufficient to establish utility. In

the instant case there is 99% homology to a protein with a well-established utility.

In Addition the Final Action argues on page 4, lines 13-15 that "While those of skill in the art may find the general assertion of utility to be believable, the general agreement of utilities the artisan would consider believable does not mane the present invention has the disclosed utilities simply because they have been asserted by Applicants." This position is in conflict with historic U.S. patent law as interpreted by the courts. In the present case, Applicants have identified sequences which encode a molecule of specific function, a molecule whose function and role in human disease is very well-known to those of skill in the art. As described in Applicants' previous response, GABA receptors, their biological role is well known to those of skill in the art, as stated in the specification "Because of their medical relevance, GABA receptors have been subject to considerable scientific scrutiny as shown in U.S. Application No. 09/183,253 (corresponding to WO9942580A2), herein incorporated by reference, which describes a variety of uses, assays, and applications" (specification at page 16, lines 9-13). Additionally, biologic roles were described in the Section 2 of the specification "GABA receptors bind potent inhibitory neurotransmitters and this interaction serves as a target for a variety of pharmaceutically active agents such as benzodiazepines, barbiturates, and alcohol" (specification at page 1, lines 26-28). Thus, clearly Applicants have asserted the sequences of the present invention encode human GABA receptors and that the biologic role of GABA receptors are well known to the art. Therefore the Examiner's position (Final Action at page 4, lines 17-19) that applicants have not identified a substantial role for this protein, how this receptor can be used or with what diseases this specific protein is associated is without merit. As is the position taken on page 5, first paragraph of the Final Action, that the amount of experimentation required to practice the claimed invention is "undue".

Applicants submit that the legal test for utility simply involves an assessment of whether those skilled in the art recognize Applicants' assertions regarding utility as credible. Recent Utility Guidelines have added that asserted utilities must be either a specific and substantial utility or a well-established utility. Clearly in the instant case, the utility is well-established, as GABA receptors, their function utility and human disease associations are very well-established. In addition Applicants have provided clear evidence that those of skill in the art would find Applicants utility assertions to be credible, because clearly they have. When faced with identifying the function of sequences that are 99% identical at the amino acid level to those of the present invention, those of skill in the art identified these sequences as

GABA receptor subunits. Applicants have asserted that the sequences of the present invention encode a GABA receptor and in a prior response provided evidence that those of skill in the art would clearly find this assertion credible. It is not the role of the Examiner to simply disregard third party scientific evidence that supports Applicants' assertions "as deemed non-persuasive". The burden is now on the Examiner to provide objective evidence that in fact the sequences of the present invention do not encode GABA receptors or that GABA receptors have no utility.

The skilled artisan would readily appreciate the utilities asserted by Appellants' regarding the role of the proteins encoded by sequences of the present invention, including those associated with diseases that have been linked to the GABA receptor. Therefore, the present utility rejection must fail. According to the Examination Guidelines for the Utility Requirement, if the applicant has asserted that the claimed invention is useful for any particular purpose (i.e., it has a "specific and substantial utility") and the assertion would be considered credible by a person of ordinary skill in the art, the Examiner should not impose a rejection based on lack of utility (66 Federal Register 1098, January 5, 2001).

In addition the Final Action also states that the Examiner does not understand how the term "anticancer activity" and "GABA receptor activity" differ (page 5, second paragraph). First Applicants note that they did not refer to the phrase GABA receptor activity, however, in attempt to clarify the issue, Applicant's respectfully submit that the phrase has GABA receptor activity is more specific than the phrase has anticancer activity. An analogous example might be that the term shortstop is more specific than the term baseball player.

As additional examples of utility for the sequences of the present invention, given that Applicants have submitted that the sequences of the present invention describe a novel gene encoding a GABA receptor subunit (which was unintentionally incorrectly identified as a GPCR in the prior response due to clerical error) and thus provide a unique identifier of the corresponding gene. However, the Final Action maintains that Appellants' assertions regarding the use of the presently claimed polynucleotides on DNA gene chips, based on the position that such a use would allegedly be generic. Further, the Examiner seems to be requiring Appellants to identify the biological role of the nucleic acid or function of the protein encoded by the presently claimed polynucleotides before the present sequences can be used in gene chip applications that meet the requirements of § 101. Appellants respectfully point out that knowledge of the exact function or role of the presently claimed

sequence is not required to track expression patterns using DNA chips. As set forth in Appellants First Response, given the widespread utility of such "gene chip" methods using *public domain* gene sequence information, there can be little doubt that the use of the presently described *novel* sequences would have great utility in such DNA chip applications.

However, clearly given the evidence that the sequences of the present invention encode a GABA receptor subunit, and given the well-established utilities described for GABA receptors and the evidence provided that the claimed sequences provide a specific marker of the gene encoding a GABA receptor subunit and as such provide a unique identifier of the corresponding gene in the human genome. Such specific markers are targets for discovering drugs that are associated with human mental disorders and diseases (specification at page 18, line 24) such as, *inter alia*, depression (specification at page 12, line 25). Thus, those skilled in the art would instantly recognize that the present nucleotide sequence would be an ideal, novel candidate for assessing gene expression using, for example, DNA chips, as the specification details at least on pages 5-7.

The Examiner is further requested to consider that, given the huge expense of the drug discovery process, even negative information has great "real world" practical utility. Knowing that a given gene is not expressed in medically relevant tissue provides an informative finding of great value to industry by allowing for the more efficient deployment of expensive drug discovery resources. Such practical considerations are equally applicable to the scientific community in general, in that time and resources are not wasted chasing what are essentially scientific dead-ends (from the perspective of medical relevance). Clearly, compositions that enhance the utility of such DNA gene chips, such as the presently claimed sequences encoding GABA Receptor subunits which Appellants have shown are well-established drug targets for mental and behavioral disorders, among others, must in themselves be useful. Moreover, the presently described protein (GABA receptor subunit) provides uniquely specific sequence resources for identifying and quantifying full length transcripts that were encoded by the corresponding human genomic locus. Accordingly, there can be no question that the described sequences provide an exquisitely specific utility for analyzing gene expression.

Although Applicants need only make one credible assertion of utility to meet the requirements of 35 U.S.C. § 101 (*Raytheon v. Roper*, 220 USPQ 592 (Fed. Cir. 1983); *In re Gottlieb*, 140 USPQ 665 (CCPA 1964); *In re Malachowski*, 189 USPQ 432 (CCPA 1976); *Hoffman v. Klaus*,

9 USPQ2d 1657 (Bd. Pat. App. & Inter. 1988)), as a further example of the utility of the presently claimed polynucleotide, the present nucleotide sequence has a specific utility in mapping the protein encoding regions of the corresponding human chromosome, as detailed in the specification Clearly, the present polynucleotide provides exquisite specificity in localizing the specific region of the human chromosome containing the gene encoding the given polynucleotide, a utility not shared by virtually any other nucleic acid sequences. In fact, it is this specificity that makes this particular sequence so useful. Early gene mapping techniques relied on methods such as Giemsa staining to identify regions of chromosomes. However, such techniques produced genetic maps with a resolution of only 5 to 10 megabases, far too low to be of much help in identifying specific genes involved in disease. The skilled artisan readily appreciates the significant benefit afforded by markers that map a specific locus of the human genome, s Only a minor percentage of the genome actually encodes exons, which in-turn encode amino acid sequences. The presently claimed polynucleotide sequence provides biologically validated empirical data (*e.g.*, showing which sequences are transcribed, spliced, and polyadenylated) that *specifically* define that portion of the corresponding genomic locus that actually encodes exon sequence. Equally significant is that the claimed polynucleotide sequence defines how the encoded exons are actually spliced together to produce an active transcript (*i.e.*, the described sequences are useful for functionally defining exon splice-junctions). The Applicants respectfully submit that the practical scientific value of expressed, spliced, and polyadenylated mRNA sequences is readily apparent to those skilled in the relevant biological and biochemical arts. For further evidence in support of the Applicants' position, the Board is requested to review, for example, section 3 of Venter *et al.* (*supra at* pp. 1317-1321, including Fig. 11 at pp. 1324-1325), which demonstrates the significance of expressed sequence information in the structural analysis of genomic data. The presently claimed polynucleotide sequence defines a biologically validated sequence that provides a unique and specific resource for mapping the genome essentially as described in the Venter *et al.* article.

As evidence of the specific utility of the sequences of the present invention in localizing the specific region of the human chromosome and identification of functionally active intron/exon splice junctions is the information provided in Applicant's previous response and associated exhibit (Exhibit F) which is the result of a sequence analysis carried out by overlaying SEQ ID NO:1 upon the identified human genomic sequence. This result indicates that the sequence of the present invention is encoded

by 11 different exons spread non-contiguously along a region of human chromosome 4 (4p12), which is represented by clones AC0095058 and AC096592. Thus clearly one would not simply be able to identify the protein encoding exons that make up the sequence of the present intention, nor to map the protein encoding regions identified specifically by the sequences of the present invention without knowing exactly what the specific sequences were. Additionally, it should be noted that the gene of Q8N1C3, Gamma-aminobutyric-acid receptor gamma-1 subunit precursor (GABA(A) receptor also maps to the same region of human chromosome 4. Thus further supporting Applicant's assertion that the sequences of the present invention encode a variant of the human GABA(A) receptor.

The Examiner has taken the position that the asserted utilities are not specific to the claimed nucleic acids and are instead general utilities that would be applicable to the broad class of nucleic acids, that virtually *any* nucleic acid can be used on a DNA chip or used to map the human chromosome (Final Action at page 6). This argument is flawed in a number of respects. First, Applicants submit that only expressed sequences can be used to track gene expression, not just any nucleic acid. Expression profiling does not require a knowledge of the function of the particular nucleic acid on the chip - rather the gene chip indicates which DNA fragments are expressed at greater or lesser levels in two or more particular tissue types. Skilled artisans already have used and continue to use sequences such as Applicants in gene chip applications without further experimentation. Second, the Examiner seems to be confusing the requirement for a **specific** utility, which is the proper standard for utility under 35 U.S.C. § 101, with the requirement for a **unique** utility, which is clearly an improper standard. As clearly set forth by the Federal Circuit in *Carl Zeiss Stiftung v. Renishaw PLC*, 20 USPQ2d 1101 (Fed. Cir. 1991):

> An invention need not be the best or only way to accomplish a certain result, and it need only be useful to some extent and in certain applications: "[T]he fact that an invention has only limited utility and is only operable in certain applications is not grounds for finding a lack of utility." *Envirotech Corp. v. Al George, Inc.*, 221 USPQ 473, 480 (Fed. Cir. 1984)

Just because other, or even more useful, polymorphic sequences from the human genome have been described does not mean that the use of the presently described polymorphic markers for forensic analysis is not a specific utility. If every invention were required to have a unique utility, the Patent and Trademark Office would no longer be issuing patents on batteries, automobile tires, golf balls, golf

clubs, and treatments for a variety of human diseases, such as cancer, just to name a few particular examples, because the utility of each of these compositions is applicable to the broad class in which each of these compositions falls: all batteries have the same utility, specifically to provide electrical power; all automobile tires have the same utility, specifically for use on automobiles; all golf balls and golf clubs have the same utility, specifically for use in the game of golf; and all cancer treatments have the same utility, specifically, to treat cancer. However, only the briefest perusal of virtually any issue of the Official Gazette provides numerous examples of patents being granted on each of the above compositions nearly every week. Furthermore, if a composition needed to be unique to be patented, the entire class and subclass system would be an effort in futility, as the class and subclass system serves solely to group such common inventions, which would not be required if each invention needed to have a unique utility. Thus, the present sequence clearly meets the requirements of 35 U.S.C. § 101.

Thus in summary, Applicants have submitted evidence that the sequences of the present invention encode, as asserted in the specification as filed, GABA receptors, whose biological function was described in the specification and is also very well-established. In contrast to the Examiner's position in the Final Action, Applicants believe that the present situation directly tracks Example 10 of the Revised Interim Utility Guidelines Training Materials (pages 53-55), which establishes that a rejection under 35 U.S.C. § 101 as allegedly lacking a patentable utility and under 35 U.S.C. § 112, first paragraph as allegedly unusable by the skilled artisan due to the alleged lack of patentable utility, is not proper when a full length sequence (such as the presently claimed sequence), and has a similarity score greater than 95% to a protein having a known function (such as the greater than 99% identity between the presently claimed sequences and those of the cited GABA receptor subunit of Q8N1C3). Furthermore this response has described a series of additional substantial, specific, credible and well-established utilities for the present invention. Therefore, Applicants submit that as the presently claimed sequence molecules have been shown to have a substantial, specific, credible and well-established utility, the rejection of the claims under 35 U.S.C. § 101 has been overcome. Thus, Applicants respectfully request that the rejection be withdrawn.

V. Rejection of Claims Under 35 U.S.C. § 112, First Paragraph

The Final Action continues to reject the claims under 35 U.S.C. § 112, first paragraph, since

allegedly one skilled in the art would not know how to use the invention, as the invention allegedly is not supported by a specific, substantial, and credible utility or a well-established utility. Applicants respectfully traverse. Applicants submit that the GABA receptor subunit encoding sequences of the present invention have been shown to have several specific, substantial, credible utility and well-established utilities, as detailed in the section above. Applicants therefore request that the rejection of the claims under 35 U.S.C. § 112, first paragraph, be withdrawn.

VI. Rejection of Claims 3 and 4 Under 35 U.S.C. § 112, First Paragraph-Enablement

The Final Action continues to reject claims 3 and 4 under 35 U.S.C. § 112, first paragraph, as allegedly not providing enablement for the full scope of the claimed invention comprising a genus of at least 80 contiguous nucleotides of SEQ ID NO:1 or 3. Applicants respectfully maintain their traverse.

In addition to the argument presented in Applicants previous response, Applicants respectfully submit that the Examiner has failed to present reasoning sufficient to establish a *prima facie* case supporting the present § 112 rejection, and accordingly the rejection is improper because: the Examiner's comments were not relevant to the established legal standard of enablement; the Examiner's failure to attribute adequate weight and attention to the detailed level of teaching clearly provided in the specification; and the reasoning for the enablement rejection provided by the Examiner failed to adequately consider the high level of technical knowledge that can be attributed to those skilled in the art in the field of the present invention.

In attempting to establish a *prima facie* case to support the § 112 rejection of the composition claims, the Final Action questions whether the claimed compositions are sufficiently enabled to allow those skilled in the art to practice aspects of the invention involving standard molecular biological techniques. The § 112 rejection, as applied against the nucleic acid compositions, is completely misplaced. It has long been established that composition claims are enabled by defining any practical use of the claimed compound. *In re Nelson*, 126 USPQ 242 (CCPA 1960); *Cross v. Iizuka, supra.* "The enablement requirement is met if the description enables any mode of making and using the invention." *Johns Hopkins Univ. v. CellPro, Inc.*, 47 USPQ2d 1705, 1719 (Fed. Cir. 1998), citing *Engel Indus., Inc. v. Lockformer Co.*, 20 USPQ2d 1300, 1304 (Fed. Cir. 1991). Thus, the

enablement issue should be resolved. Enablement only requires that the specification describe a practical use for the composition defined in the claims, and that a skilled artisan be able to make and use the claimed DNA segments without undue experimentation.

The Final Action seems to contend that the specification provides insufficient guidance regarding the biological function or activity of certain of the claimed compositions. However, such an enablement standard conflicts with established patent law and furthermore, in fact, the specification provides the clear assertion that the sequences of the present invention encode a GABA receptor. Those of skill in the art agree that the sequences of the present invention encode a GABA receptor and GABA receptors are very well-known to those of skill in the art with well-established utilities including as drug targets. Thus information obtained using, for example, DNA chips would be extremely useful and would be readily recognized as such by those of skill in the art.

The Final Action argues essentially that though a first nucleic acid may share identical regions with a second nucleic acid, it is highly unpredictable as to whether the two nucleic acids encode proteins having identical functions. However, this argument is misplaced, first, because all species of an invention are not required to have the exact same function, and second, because numerous uses of the claimed sequences do not require knowledge of any functional aspects of the amino acid sequences. Applicants point out that significant commercial exploitation of nucleic acid sequences requires no more information than the nucleic acid sequence itself. Applications ranging from gene expression analysis or profiling (utilizing, for example, arrays of short, overlapping or non-overlapping, oligonucleotides and DNA chips, as described above) to chromosomal mapping (utilizing, for example, short oligonucleotide probes or full length DNA sequences, as described above) are practiced utilizing nucleic acid sequences and techniques that are well-known to those of skill in the art. The widespread commercial exploitation of nucleic acid sequence information points to the level of skill in the art, and the enablement provided by disclosures such as the present specification, which include specific nucleic acid sequences and guidance regarding the various uses of such sequences.

Even though the burden has been improperly shifted to Applicants, the following section is being provided to demonstrate that the specification is fully enabling in view of the detailed guidance and teaching provided in the specification within the context of the high level of technical knowledge present in the art regarding the use of nucleic acids such as those presently claimed.

The Final Action questions the teaching and guidance in the specification for certain aspects of the present invention. However, as discussed above, this requirement is completely misplaced. There is sufficient knowledge and technical skill in the art for a skilled artisan to be able to make and use the claimed DNA species in a number of different aspects of the invention entirely without further details in a patent specification. For example, it is not unreasonable to expect a Ph.D. level molecular biologist to be able to use the disclosed sequence to design oligonucleotide probes and primers and use them in, for example, PCR based screening and detection methods to obtain the described sequences and/or determine tissue expression patterns. Nevertheless, the present specification provides highly detailed descriptions of techniques that can be used to accomplish many different aspects of the claimed invention, including recombinant expression, site-specific mutagenesis, *in situ* hybridization, and large scale nucleic acid screening techniques, and properly incorporates by reference a montage of standard texts into the specification, such as Sambrook *et al.* (*Molecular Cloning, A Laboratory Manual*) and Ausubel *et al.* (*Current Protocols in Molecular Biology*) to provide even further guidance to the skilled artisan. Incorporation of material into the specification by reference is proper. *Ex parte Schwarze*, 151 USPQ 426 (PTO Bd. App. 1966). The § 112, first paragraph rejection is thus *prima facie* improper:

> As a matter of patent office practice, then, a specification disclosure which contains a teaching of the manner and process of making and using the invention in terms which correspond in scope to those used in describing and defining the subject matter sought to be patented must be taken as in compliance with the enabling requirement of the first paragraph of § 112 unless there is reason to doubt the objective truth of the statements contained therein which must be relied on for enabling support.

In re Marzocchi & Horton, 169 USPQ 367, 369 (CCPA 1971), emphasis as in original. In any event, an alleged lack of express teaching is insufficient to support a first paragraph rejection where one of skill in the art would know how to perform techniques required to perform at least one aspect of the invention. As a matter of law, it is well settled that a patent need not disclose what is well known in the art. *In re Wands, supra.* In fact, it is preferable that what is well known in the art be omitted from the disclosure. *Hybritech, Inc. v. Monoclonal Antibodies, Inc.*, 231 USPQ 81 (Fed. Cir. 1986). As standard molecular biological techniques are routine in the art, such protocols do not need to described in detail in the specification.

Furthermore, a specification "need describe the invention only in such detail as to enable a person skilled in the most relevant art to make and use it." *In re Naquin*, 158 USPQ 317, 319 (CCPA 1968); emphasis added. The present claims are thus enabled as they are supported by a specification that provides sufficient description to enable the skilled person to make and use the invention as claimed.

As detailed in the sections above, all aspects of the enablement rejection under 35 U.S.C. § 112, first paragraph have been overcome, particularly as the specification provides the clear assertion that the sequences of the present invention encode a GABA receptor, those of skill in the art agree and GABA receptors are very well-known to those of skill in the art with well-established utilities. Applicants therefore respectfully request that the rejection be withdrawn.

VII. Rejection of Claims 3 and 4 Under 35 U.S.C. § 112, First Paragraph-Written Description

The Final Action states that claims 3 and 4 fail to meet the written description requirement because "Applicants have not identified what the function of theses nucleic acid molecules is in order to characterize and limit this genus"(the Final Action at page 9). While the Final Action admits that the claims in fact do include a distinguishing feature, specifically, that the nucleic acid molecule must "comprise at least 80 consecutive nucleotides of SEQ ID NO:1 or 3" (the Final Action at page 8). However, the Action views this structural feature as insufficient "The only structural description provided..." Applicants respectfully point out that this is all that is required of claims to meet the written description requirement of 35 U.S.C. § 112, first paragraph.

The Final Action suggests that a stretch of at least 80 consecutive nucleotides of SEQ ID NO:1 or 3 is not a meaningful structural limitation and a distinguishing feature, because such a limitation does not require that the nucleic acid molecules possess any particular biological activity, nor any particular conserved structure, or other distinguishing feature (the Final Action at page 8). Applicants point out that **every aspect** of this argument fails to take into consideration the proper basis for compliance with the written description requirement under 35 U.S.C. § 112, first paragraph. First, the Examiner seems to be requiring that the structural limitation of "at least 80 consecutive nucleotides of SEQ ID NO: 1 or 3" have a functional basis, specifically that it possess a "particular biological activity". This argument

completely defies logic - of course this **structural** limitation does not have a functional basis. Second, the limitation of "at least 80 consecutive nucleotides of SEQ ID NO:1 or 3" does in fact have a particular conserved structure, specifically, each and every species is conserved within the nucleotide sequence of SEQ ID NO:1 or 3. Thus, these species are each unique markers of the nucleotide sequence of SEQ ID NO:1 or 3. Thus, the Examiner's argument in no way supports the allegation that claims 3 and 4 do not meet the written description requirement under 35 U.S.C. § 112, first paragraph.

35 U.S.C. § 112, first paragraph, requires that the specification contain a written description of the invention. The Federal Circuit in *Vas-Cath Inc. v. Mahurkar* (19 USPQ2d 1111 (Fed. Cir. 1991); "*Vas-Cath*") held that an "applicant must convey with reasonable clarity to those skilled in the art that, as of the filing date sought, he or she was in possession *of the invention.*" *Vas-Cath*, at 1117, emphasis in original. However, it is important to note that the above finding uses the terms reasonable clarity to those skilled in the art. Further, the Federal Circuit in *In re Gosteli* (10 USPQ2d 1614 (Fed. Cir. 1989); "*Gosteli*") held:

> Although [the applicant] does not have to describe exactly the subject matter claimed, ... the description must clearly allow persons of ordinary skill in the art to recognize that [he or she] invented what is claimed.

Gosteli at 1618, emphasis added. Additionally, *Utter v. Hiraga* (6 USPQ2d 1709 (Fed. Cir. 1988); "*Utter*"), held "(a) specification may, within the meaning of 35 U.S.C. § 112 ¶1, contain a written description of a broadly claimed invention without describing all species that claim encompasses" (*Utter*, at 1714). Therefore, all Applicants must do to comply with 35 U.S.C. § 112, first paragraph, is to convey the invention with reasonable clarity to the skilled artisan.

Further, the Federal Circuit has held that an adequate description of a chemical genus "requires a precise definition, such as by structure, formula, chemical name or physical properties" sufficient to distinguish the genus from other materials. *Fiers v. Revel*, 25 USPQ2d 1601, 1606 (Fed. Cir. 1993; "*Fiers*"). *Fiers* goes on to hold that the "application satisfies the written description requirement since it sets forth the ... nucleotide sequence" (*Fiers* at 1607). In other words, provision of a structure and formula - the nucleotide sequence - renders the application in compliance with 35 U.S.C. § 112, first paragraph.

More recently, the standard for complying with the written description requirement in claims involving chemical materials has been explicitly set forth by the Federal Circuit:

> In claims involving chemical materials, generic formulae usually indicate with specificity what the generic claims encompass. One skilled in the art can distinguish such a formula from others and can identify many of the species that the claims encompass. Accordingly, such a formula is normally an adequate description of the claimed genus. *Regents of Univ. of California v. Eli Lilly and Co.*, 43 USPQ2d 1398, 1406 (Fed. Cir. 1997).

Thus, a claim describing a genus of nucleic acids by structure, formula, chemical name or physical properties sufficient to allow one of ordinary skill in the art to distinguish the genus from other materials meets the written description requirement of 35 U.S.C. § 112, first paragraph. As further elaborated by the Federal Circuit in *Regents of Univ. of California v. Eli Lilly and Co.*:

> In claims to genetic material ... a generic statement such as 'vertebrate insulin cDNA' or 'mammalian insulin cDNA', without more, is not an adequate written description of the genus because it does not distinguish the claimed genus from others, except by function. It does not specifically define any of the genes that fall within its definition. It does not define any structural features commonly possessed by members of the genus that distinguish them from others. One skilled in the art cannot, as one can do with a fully described genus, visualize or recognize the identity of members of the genus. (Emphasis added)

Thus, as opposed to the situation set forth in *Regents of Univ. of California v. Eli Lilly and Co.* and *Fiers*, the nucleic acid sequences of the present invention are not distinguished on the basis of function, or a method of isolation, but in fact are distinguished by structural features - a chemical formula, *i.e.*, the *sequence itself.*

Using the nucleic acid sequences of the present invention (as set forth in the Sequence Listing), the skilled artisan would readily be able to **distinguish** the claimed nucleic acids from other materials on the basis of the specific **structural** description provided. Polynucleotides comprising at least 80 contiguous bases from SEQ ID NO: 1 or 3 are within the genus of the instant claims, while those that lack this structural feature lie outside the genus. The claimed genus of polynucleotides is clearly defined in structural terms, which is **all that is required** of claims 3 and 4 to meet the written description requirement of 35 U.S.C. § 112, first paragraph.

For each of the foregoing reasons, Applicants submit that the rejection of claims 3 and 4 under 35 U.S.C. § 112, first paragraph has been avoided and should be withdrawn.

VIII. Conclusion

The present document is a full and complete response to the Final Action. In conclusion, Applicants submit that, in light of the foregoing remarks, the present case is in condition for allowance, and such favorable action is respectfully requested. Should Examiner Landsman have any questions or comments, or believe that certain amendments of the claims might serve to improve their clarity, a telephone call to the undersigned Applicants' representative is earnestly solicited.

Respectfully submitted,

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Date

Lance K. Ishimoto Reg. No. No. 41,866
Agent for Applicants

LEXICON GENETICS INCORPORATED
(281) 863-3333

Customer # 24231